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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,326	03/20/2006	John Nicholas Staniforth	478.1073	8789

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,326	STANIFORTH ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-9,14-37,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-9,14-37,39 and 40* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/17/06; 10/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 6-9, 14-37, and 39-40 are pending. Applicants amended claims 1, 46, 9, 24, 28, 32, and 37. Applicants cancelled claims 5 and 10-13. Receipt and consideration of Applicants two IDS's (submitted 10/7/05 and 7/17/06), amended claim set, and remarks/arguments submitted on October 29m 2009 are acknowledged.

Election/Restrictions

Applicant's election without traverse of (i) passive dry powder inhaler as the kind of dry powder inhaler, (ii) metal stearates as the kind of additive material, and (iii) small molecule as the kind of active agent in the reply filed on October 29, 2009 is acknowledged. Applicants' elected species read on all the pending claims as amended by Applicants.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country. It appears Applicants may be trying to claim priority to GB 03216124 filed on September 15, 2003 in Great Britain.

Specification

The specification is objected to because it is missing a sections entitled, (a) "Cross-References to Related Applications" and (b) "Brief Summary of the Several Drawings" A description of what these missing sections should contain is below:

Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11

Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Devices and pharmaceutical compositions for enhancing dosing efficiency comprising apomorphine and force control agents, such as metal stearates.

Claim Objections

Claim 20 is objected to because of the following informalities: the words "is reached" should be inserted in line 1 of claim 20 between the words "level" and "within," respectively. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6-9, 14-37, and 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing, because it states that the dry powder inhaler comprises a dry powder formulation comprising apomorphine and a metal stearate [i.e. a constituent component of the DPI is the dry powder]; however, Applicants' specification states in paragraph [0050] that the dry powder inhalers ***contain*** a dry powder formulation. It is not physically possible for the dry powder inhaler to comprise a dry powder composition and also to deliver this composition upon actuation; but it is possible for the dry powder inhaler to contain a dry powder composition and deliver said composition upon actuation.

Claim 3 is vague and indefinite, because it is unclear whether a dosing efficiency at 2 microns of at least 40% is a required claim limitation, due to the presence of the word "preferably" on line 2 of claim 3, before the phrase, "at least 40% is achieved." Appropriate correction and clarification are required.

Claim 6 is vague and indefinite, because on line 2 it utilizes "means + function" language, and thus invoke the provisions of 35 U.S.C. § 112, 6th paragraph. However, Applicants' specification does not identify what the suitable means for producing droplets are that are part of the spray drier. Thus, Applicants' claim is indefinite, because Applicants'

specification fails to define the suitable means to accomplish the recited function of producing droplets.

Claim 9 is vague and indefinite, because it is unclear how the method of the recited product-by-process limitation is utilized.

Claim 21 recites the limitation "the pharmacodynamic effect" in line 2. There is insufficient antecedent basis for this limitation in the claim. There is no reference in parent claim 1 to "a pharmacodyanmic effect."

Claim 32 is vague and indefinite, because the phrase “adverse side effects normally associated with administration of apomorphine via other routes" is ambiguous. The ordinary skilled artisan would not be unable to ascertain the metes and bounds of adverse side effects "associated with..." nor would the ordinary skilled artisan be able to unambiguously ascertain what is meant by “normally associated.” The phrase “normally associated with” is not defined in Applicants’ specification and the claims do not elucidate the intended meaning of this phrase. Appropriate correction and clarification are required.

The remaining claims are rejected as depending from a rejected claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 9, 14-37, and 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth et al. (US 2004/0204439).

Applicant Claims

Applicants claim a passive dry powder inhaler (passive DPI) device comprising [sic] a dry powder formulation comprising apomorphine and a metal stearate.\

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Staniforth teaches **inhalable dry powder compositions** comprising (i) apomorphine or pharmaceutically acceptable salts thereof, wherein **at least 90% of the apomorphine has a particle size of 5 microns or less**, (ii) carrier material having an average particle size of from

about 40 to about 70 microns, and in some embodiments the compositions may also comprise (iii) **force control agents, such as magnesium stearate (i.e. a metal stearate)** (title; abstract; [0010]; [0024]-[0025]; [0065], and [0090]-[0092]). For effective administration by a dry powder inhaler the particles of apomorphine are sufficiently fine such that **at least 35%, preferably at lest 45%, more preferably at least 50%; and most preferably at least 60% of the apomorphine particles are delivered upon actuation from a dry powder inhaler** [0073]-[0074]. The powder compositions may be administered from active **or passive dry powder inhalers** [0065], wherein examples of **commercially available suitable passive dry powder inhalers include rotohaler, diskhaler, or turbohaler (a multidose passive dry powder inhaler)** ([0065] and[0086]). The term "fine particle fraction" is defined in paragraph [0075] to mean the fraction of the total amount of active material delivered by a device which has a diameter of not more than 5 microns. Staniforth exemplifies **a 200 mg dry powder composition comprising (i) 20.00% w/w apomorphine HCl, (ii) 79.75% w/w lactose, and (iii) 0.25% magnesium stearate**, in Example 9 ([00163]-[0164]), wherein the composition is made according to the method of Example 2 ([0132]-[[0136]). The compositions may be stored in a blister of a blister pack [0070]. Storage of the compositions in one or more blisters, reads on a pre-metered dose, and meets the limitations of claim 14.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Staniforth does not anticipate the rejection claims, because Staniforth does not exemplify a passive dry powder inhaler (passive DPI) containing a formulation comprising apomorphine and a metal stearate. Staniforth's teachings, however, are suggested of the claimed invention.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious to a person of ordinary skill at the time of the instant invention to place a dry powder composition comprising (i) apomorphine or a pharmaceutically acceptable salt thereof, (ii) carrier particles, and (iii) a force control agent, such as magnesium stearate, into a blister, blister pack, or within a single dose passive dry powder inhaler, because Staniforth's teachings are explicitly disclose the aforementioned dry powder composition and explicitly states that invented compositions can be administered to a patient from a passive dry powder inhaler. An ordinary skilled artisan would have been motivated to follow Staniforth's teachings regarding suitable means of administering the invented powders to obtain a reasonable expectation of successful 'inhalation administration of apomorphine dry powder formulation to a patient in need thereof, such as to a patient in need of treatment of a sexual dysfunction. Regarding the pharmacodynamic properties recited in dependent claims 19-32 and 37, these properties are reasonably expected to result from inhalation administration of Staniforth's apomorphine formulations, because the prior art suggests the inhalation administration of compositions comprising the same required components of apomorphine and a metal stearate. Regarding the recited dosing efficiency and emitted dose in dependent claims 2-3 and 15-18, these properties will necessarily result from the administration of Staniforth's invented apomorphine compositions from a passive inhaler, because Staniforth teaches compositions comprising the same required components of apomorphine and a metal stearate Staniforth's compositions are not made in a method utilizing any solvents (see Example 2 cited above). Regarding the product-by-process limitations of spray drying to obtain the dry powder formulation contained in the claimed passive dry powder inhaler, this limitation is given little

weight, because the only structural feature imparted by spray drying is understood to be the recited particulate nature of the apomorphine dry powder composition. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 and 19-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 21, 24, 26, 42, and 44 of copending Application No. 10/552,231 (copending '231). Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets recite or claim apomorphine compositions comprising apomorphine and a metal stearate.

Independent claim 1 of the instant application is described above. Dependent claim 26 of copending '231 claims a composition for pulmonary inhalation comprising (i) apomorphine in an amount to provide a nominal dose of from about 100 to about 1600 micrograms of apomorphine and (ii) from about 0.15% w/w to about 5% w/w of an additive selected from a group consisting of leucine, magnesium stearate, lecithin, and sodium stearyl fumarate. Both magnesium stearate and sodium stearyl fumarate are metal stearates.

The primary difference between dependent claim 26 of copending '231 and the claims of the instant application is that dependent claim 26 of copending '231 does not recite that the composition is contained within a passive dry powder inhaler (i.e. a breath-actuated DPI) or that the apomorphine composition has a dosing efficiency at 5 microns of at least 70%. Dependent claims 21 and 24 of copending '231 establish that it is an obvious modification of the claimed composition of copending '231 to formulate the composition where the apomorphine is in the form of particles having a MMAD of 5 microns or less. It is the Examiner's position that the apomorphine particulate composition comprising apomorphine and a metal stearate and having a MMAD of 5 microns or less would necessarily exhibit the recited dosing efficiency. Dependent claims 42 and 44 of copending '231 establish that an obvious modification of the claims of copending '231 would be to place said compositions within a passive DPI (i.e. a breath-actuated inhaler device). Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-4 and 6-7 *prima facie* obvious claims 1, 21, 24, 26, 42, and 44 of copending Application No. 10/552,231 (copending '231).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4 and 19-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 99-100 of copending Application No. 12/459,686 (copending '686) in view of Staniforth et al. (US 2004/0204439).

Independent claim 1 of the instant application is described above. Dependent claim 100 of copending '686 claims a composition for pulmonary inhalation comprising (i) apomorphine in an amount to provide a nominal dose of from about 100 to about 600 micrograms of apomorphine, (ii) from about 0.1% w/w to about 10% w/w of a carrier material, and (iii) a force control agent selected from a group consisting of leucine, magnesium stearate, lecithin, and sodium stearyl fumarate. Both magnesium stearate and sodium stearyl fumarate are metal stearates.

The primary difference between dependent claim 100 of copending '686 and the claims of the instant application is that dependent claim 100 of copending '686 does not recite that the composition is contained within a passive dry powder inhaler (i.e. a breath-actuated DPI) or that the apomorphine composition has a dosing efficiency at 5 microns of at least 70%. These deficiencies are cured by the teachings of Staniforth set forth above. Thus, it would be a prima facie obvious modification of claim 100 of copending '686 in view of the teachings of Staniforth to place the composition of claim 100 of copending '686 within a passive dry powder inhaler and to use particulate apomorphine having a dosing efficiency at 5 microns of at least 70%. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-4 and 19-32 *prima facie* obvious claims 1, 21, 24, 26, 42, and 44 of copending Application No. 10/552,231 (copending '231).

This is a provisional obviousness-type double patenting rejection.

Conclusion

Claims 1-4, 6-9, 14-37, and 39-40 are rejected. Claim 20 and the specification are objected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, ~10:00-6:00 and Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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